DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room –WO66-G609
Silver Spring, MD 20993-0002

SEP 16 2010

Mr. Daniel Flaig
Regulatory Affairs
Boston Scientific Corporation
4100 Hamline Avenue North
St. Paul, Minnesota 55112-5798

Re: P010012 / S230
Cognis CRT-D Models N118, N119
Livian CRT-D Models H220, H225, H227 and H229
Contak Renewal 3 RF HE CRT-D Models H210, H215, H217, H219
Filed: December 11, 2009
Amended: March 2, March 5, April 12, April 30, May 27, 2010
Procode: NIK

Dear Mr. Flaig:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) supplement for a modification to the indications for use for the Cognis CRT-D Models N118, N119; Livian CRT-D Models H220, H225, H227 and H229; and Contak Renewal 3 RF HE CRT-D Models H210, H215, H217, H219 Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) as follows:

These Boston Scientific Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) are indicated for patients with heart failure who receive stable optimal pharmacologic therapy (OPT) for heart failure and who meet any one of the following classifications:

- Moderate to severe heart failure (NYHA Class III-IV) with EF $\leq$ 35% and QRS duration $\geq$ 120 ms
- Left bundle branch block (LBBB) with QRS $\geq$ 130 ms, EF $\leq$ 30%, and mild (NYHA Class II) ischemic or nonischemic heart failure or asymptomatic (NYHA Class I) ischemic heart failure

We are pleased to inform you that the PMA supplement is approved. You may begin commercial distribution of the devices as modified in accordance with the conditions of approval described below.

The sale and distribution of these devices are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The devices are further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the devices. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the devices. Your devices are therefore restricted devices subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for these devices have been established and approved at one year. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" (please use this title even if the specified interval is more frequent than one year) and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the devices, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the devices.

In addition, because your devices are pacemakers, implantable cardioverter-defibrillators (ICD), or system leads, FDA has determined that the following additional information is necessary to provide continued reasonable assurance of the safety and effectiveness of the devices. In the Annual Report, provide the following information known by or reported to the applicant:

1. The number of pulse generators domestically implanted and the number of reported explants and deaths.

2. A breakdown of the reported deaths into pulse generator related and non-pulse generator related.

3. A breakdown of the reported explants into the number reported that were:

a. For pacemakers and pulse generators: at end of battery life, the number that had complications not resolvable by programming, and, as applicable, the numbers that experienced other safety and effectiveness complications as ascertained by the user, applicant, or otherwise, or

b. For leads: associated with mechanical failure, associated with clinical complications, and as applicable, the numbers that experienced other safety and effectiveness complications as ascertained by the user, applicant, or otherwise.

4. The number of pulse generators returned to the applicant for cause from domestic sources, with a breakdown into:

a. For pacemakers and pulse generators: the number currently in analysis, the number operating properly, and the number at normal battery depletion and failed (with the failure mechanisms described).

b. For leads: the number currently in analysis, the number operating properly, the number failed (with failure mechanisms described); broken down into groupings for full leads and partial leads.

5. A cumulative survival table for the pulse generators.

In addition to the Annual Report requirements, you have agreed to provide the following data in a separate post-approval study report. As a condition of approval, you have agreed to conduct the following post-approval studies:

1) *PAS I: MADIT-CRT PAS in American College of Cardiology National Cardiovascular Data Registry (NCDR)*
This study is to be conducted comparing CRT-D performance to that of ICD within the NCDR of patients that meet the newly expanded indication for BSC CRT-D systems. The study is designed to confirm the mortality reduction observed in the MADIT-CRT study associated with the use of CRT-D when compared to ICD in patients with a LBBB conduction disturbance. The MADIT-CRT PAS in NCDR PAS (PAS I) will consist of

a. a CRT-D group: Patients implanted with a Boston Scientific CRT-D device after the MADIT-CRT indication approval date;
b. an ICD control group: Patients implanted with a Boston Scientific ICD; either,
   i. after the MADIT-CRT indication approval date, or,
   ii. before the MADIT-CRT indication approval date. a post-approval study duration of at least 5 years;
c. A minimum of 1300 patients who meet the specified criteria; have been implanted with a Boston Scientific CRT-D device followed for a minimum of 5 years;
d. A minimum of 1300 patients who meet the specified criteria; have been implanted with a Boston Scientific ICD device followed for a minimum of 5 years;
e. A minimum of 500 Class I patients who meet the specified criteria, including a

minimum of 225 who have been implanted with a with a Boston Scientific CRT-D device, have been identified and followed for a minimum of 5 years;

f. a hypothesis driven primary objective for the study designed to evaluate the effect of CRT-D, compared to ICD, on the time-to-all-cause mortality within 5 years post implant;
g. an evaluation of the differences in baseline characteristics between the CRT-D and ICD groups;
h. post-approval study status reporting at least every 6 months.

2) *PAS II: MADIT-CRT Post Approval Registry*
This study is an extended follow-up phase in the MADIT-CRT patient population to evaluate the five-year all-cause mortality rate in CRT-D vs. ICD in the MADIT-CRT patient population. The MADIT-CRT Post Approval Registry (PAS II) will consist of:

a. a registry by a maximum of 87 centers including up to 640 CRT-D patients and 426 ICD patients (or the number of patients still actively followed in the respective treatment arms at the close of the MADIT-CRT IDE study) followed out to five years post implant;
b. cox proportional hazards regression analysis of mortality, adjusting for relevant risk factors analyzed with the following approaches;
    i. on an intention-to-treat-basis (without regard to device actually implanted),
    ii. similarly but censoring follow-up when a patient first crosses over to a different device, and
    iii. by a full efficacy analysis identifying, to the extent feasible, daily utilization of an active CRT-D, an ICD-only or no active device;
c. heart failure event analysis where first heart failure events will be analyzed by Cox proportional hazards modeling and subsequent heart failure events analyzed by Andersen-Gill proportional intensity modeling;
d. post-approval study status reporting at least every 6 months;

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

FDA would like to remind you that you are required to submit PAS Progress Reports every six months. The PAS Progress Reports should be submitted separately from the Annual Reports. Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order"
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm

Before making any change affecting the safety or effectiveness of the devices, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for these devices. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such devices or similar devices marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of these devices initiated by you to: (1) reduce a risk to health posed by the devices; or (2) remedy a violation of the act caused by the devices which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Dockets Management Branch, (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory

committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your devices, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (general information: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm; clinical and statistical data: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm)

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If you have any questions concerning this approval order, please contact Ken Skodacek at 301-796-6364.

Sincerely yours,

Matthew C. Falk MD PhD for

Christy Foreman
Acting Director
Office of Device Evaluation
Center for Devices and Radiological Health